For patients with potentially curable limited stage SCLC, concurrent administration of myeloid growth factors with chemotherapy and radiation has led to paradoxical worsening of cytopenias, presumably related to radiation damage of CSF mobilized peripheral blood stem cells. This remains a poorly studied area. Carefully done studies that vary the timing of myeloid growth factors in relationship to chemotherapy and radiation might be very informative.

For NSCLC, in the era of platinum based treatment in patients with advanced disease, a survival benefit has clearly been shown, but it is quite modest in nature. Therefore, with the perceived lower benefit of chemotherapy in NSCLC, there has also been an intent to minimize toxicity, often by altering dose and schedule of chemotherapy. In the case of paclitaxel, switching from prolonged infusions to short infusions reduced the duration of neutropenia. Other regimens have moved to weekly administration rather than every three weeks which also allow one to titrate or eliminate the subsequent doses that may worsen myelosuppression. Interestingly, even in advanced stage NSCLC, the development of neutropenia is associated with a longer survival compared to patients who do not have neutropenia. While neutropenia may be telling us about pharmacogenomics, it suggests that dose may be an important variable, even on advanced stage lung cancer patients, and this may have implications for chemotherapy in earlier stage disease.

Now that adjuvant chemotherapy has become a standard part of practice in Stage IB, III NSCLC, it is important to fully understand the relationship of dose and schedule to outcome. In this curative setting, it is also important to understand which patients are most at risk for neutropenia and who might benefit from early intervention strategies. The ANC Study Group has developed a risk model for factors associated with the likelihood of neutropenic complications, febrile neutropenia and dose reduction. These models now need to be applied prospectively in selected populations. The need for such a prospective risk model is also important for patients with more advanced NSCLC. Because the individual risk is low, first cycle prophylaxis is not commonly applied. However, because a large number of patients treated with NSCLC have co-morbidities, the number of NSCLC patients hospitalized with febrile neutropenia is substantial. Furthermore, the clinical course for patients with febrile neutropenia in the setting of lung cancer is more similar to patients with hematologic malignancies than with other solid tumors such as breast cancer. Although the reasons for this are not fully explored, advanced age and co-morbidity may account for the higher mortality rate from febrile neutropenia, as well as need for prolonged hospitalization in many patients. Therefore, identifying patients at risk not only for febrile neutropenia, but for prolonged complications is another important area for study.

Session E11: Controversy in Small Cell Lung Cancer

E11-01 **Controversy in Small Cell Lung Cancer, Tue, Sept 4, 16:00 – 17:30**

Controversy in small cell lung cancer - staging

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Staging of cancers has traditionally been based on the requirement to accurately define patients with localised disease that can be treated with surgical resection with curative intent. For certain malignancies, this involves defining involvement of regional lymph nodes that can be resected in continuity with the primary or separately. The finding of metastatic disease beyond regional nodes alters the treatment to primarily systemic and in most solid tumours from cure to palliation.

Small cell lung cancer challenges this paradigm. Prior to the introduction of systemic therapy, there was no realistic curative approach for localised disease, with case series reporting median survivals of less than 2 months with surgery and/or radiation. The introduction of multi-agent systemic chemotherapy substantially extended median survival both in patients with metastatic disease and in those with apparent localised disease. However, the finding that radiation therapy could significantly enhance the outcome of systemic chemotherapy, particularly the longer term survival chances, results in the primary goal of SCLC 'staging' being the determination on whether thoracic radiation therapy is appropriate or not. Thus 'limited' SCLC is not a staging that directly reflects T and N stage, but a definition based on the ability to treat a patient with radiation therapy fields that encompass the tumour volume. Determining the extent of intrathoracic disease is only important when it removes the possibility of 'encompassing' by radiation fields, for example finding a malignant pleural effusion. Minor nuances, such as whether contralateral mediastinal nodes are 'limited' or 'extensive', are not relevant.

The search for 'extensive' SCLC has progressively followed advances in diagnostic imaging. Since the 1970s, CT scanning, nuclear bone scans, MRI scanning, and F18-FDG-PET scanning have been applied to identify sites of disease in SCLC patients and all have reported the ability to detect disease otherwise missed and so 'upstage' patients to extensive disease. Integrated PET/CT scanning has not been reported in detail in SCLC but is likely to improve the accuracy of PET scanning in SCLC also. The replacement of multiple staging investigations by a single investigation is likely to reduce costs and patient inconvenience and PET/CT may provide this particularly if adequate images of the brain can be obtained. PET scanning can also potentially aid radiation therapy planning in SCLC, as in NSCLC, by defining central tumour mass versus collapsed lung, and detecting involvement of anatomically normal lymph nodes.

While routine bone marrow biopsies are no longer part of SCLC staging, studies that have examined bone marrow by more refined techniques than routine H & E staining have reported much higher detection of malignant cells than is otherwise the case. In the era when high dose therapy and stem cell transplant were being investigated for SCLC treatment, a high incidence of detecting circulating tumor cells in peripheral blood was reported. It is therefore likely that there is no such thing as truly 'limited' SCLC, but all patients have 'extensive disease' that could be detected by more refined diagnostic imaging and/or molecular pathology.

Therefore the goal of staging a patient with SCLC is not defining anatomical disease parameters but deciding whether a sufficiently large percentage of the burden of tumour cells are anatomically situated where delivery of a sufficient dose of radiation therapy to potentially eradicate chemotherapy-resistant clones is possible. This is dependent not only on staging but to some extent on the judgement of the radiation oncologist and will alter with advances in techniques of radiation delivery and planning. Use of a TNM-type staging paradigm in SCLC does not reflect either disease biology or direct treatment, so is not appropriate.